REMARKS

Applicant's counsel wish to express their appreciation for the courtesies extended during the December 6, 2001 interview with the Examiner. During this interview the Examiner requested that Applicant identify scientific articles that show the relationship between acid-related gastrointestinal disorders and the disorders included in claims 656, and 719. In response, Applicant encloses the following articles which are included in the Information Disclosure Statement on file:

(i) Chi-Kong, *et al.*, Antacids Indications and Limitation, Drugs 47 (2), 305-317, 1994;

(ii) P. Jungnickel, Pantoprazole: A New Proton Pump Inhibitor, Clinical Therapeutics, Vol. 22, No. 11, 1268-1293, 2000.

(iii) G. Larson, *et al.*, Gastric Response to Severe Head Injury, The American Journal of Surgery, Vol. 47, 97-105, January 1984.

(iv) P. Roy, *et al.*, Zollinger-Ellison Syndrome Clinical Presentation in 261 Patients, Medicine, Vol. 79, No. 6, 379-411, 2000. data no good

Chi-Kong, *et al.* describe peptic ulcer disease, gastroesophageal reflux disorder, duodenal ulcer disease, stress ulcer syndrome, and dyspepsia. P. Jungnickel describes duodenal ulcer disease, gastric ulcer disease, Zollinger-Ellison Syndrome, gastroesophageal reflux disease, and erosive esophagitis. And both G. Larson, *et al.*, and P. Roy, *et al.* describe pathological gastric acid hypersecretion.

Applicant respectfully submits that no new matter has been added by the amendments to the claims or by the addition of new claims.

Support for claim 23 can be found at least on page 24, lines 16-19; on page 26, lines 25-27; on page 28, lines 18-21; on page 32, lines 1-5; and on page 35, lines 11-13, of the specification.

Support for claims 27-33, 104-110, 634, 641, 688, 695, 730, and 737 can be found at least on page 26, lines 18-24, of the specification.

Support for claims 34, 112, and 652 can be found at least on page 33, lines 12-16, of the specification.

Support for claims 35, and 113 can be found at least on page 33, lines 12-17, of the specification.

Support for claims 38, 39, 42, 43, 114-117, 119-123, 649, and 703 can be found at least on page 24, lines 15-19, of the specification.

Support for claims 40, 118, 653, 704, 745, and 759 can be found at least on page 45, line18, of the specification.

Support for claims 52, 53,130, 131, 625, 626, and 679-681 can be found at least on page 43, line 11, of the specification.

Support for claims 65, 69, 73, 81, 84, 135, 662, 717, and 725 can be found at least on page 34, line 16, through page 35, line 11, of the specification.

Support for claim 95 can be found at least on page 24, lines 16-19; on page 26, lines 25-27; on page 27, lines 19-31; on page 32, lines 1-5; and on page 35, lines 11-13, of the specification.

Support for claims 95, 96, 656, 718, and 719 can be found at least on page 27, lines 19-31, of the specification.

Support for claims 95, and 718 can be found at least on page 28, line 30, through page 29, line 2, of the specification.

Support for claims 127, 664, 755, and 862 can be found at least on page 31, lines 22-25, of the specification.

Support for claims 128, 622, and 863 can be found at least on page 30, line 31, to page 31, line 14, of the specification.

Support for claims 129, 624, and 864 can be found at least on page 31, lines14-17; and on page 43, lines 12-17, of the specification.

Support for claims 132-133, 627-629, 682-685, can be found at least on page 43, line 12, of the specification.

Support for claims 134, and 686 can be found on at least on page 37, lines 21-28, of the specification.

Support for claim 137 can be found at least on page 31, lines 28-31, of the specification.

Support for claim 138 can be found at least on page 49, lines 7-9, and on page 58, lines 27-30, of the specification.

Support for claims 630-632 can be found on at least on page 28, lines 18-21, on page 32, lines 1-5, and on page 47, lines 25-28, of the specification.

Support for claims 633, 635-640, 642-647, 687, 689-694, 696-701, 729, 731-736, 738-743, and 757 can be found at least on page 28, lines 18-27, of the specification.

Support for claims 648, 702, 744, 758, can be found at least on page 38, lines 14-16, of the specification.

Support for claims 650 can be found at least on page 42, lines 26-31, of the specification.

Support for claims 653, 704, 745, and 759 can be found at least on page 33, lines 12-16; on page 43, lines 10-26,and on page 33, lines 12-16, of the specification.

Support for claims 654, 716, and 746 can be found at least on page 24, lines 27-29, of the specification.

Support for claims 661, 724, and 765 can be found at least on page 78, lines 11-14, of the specification.

Support for claim 666 can be found at least on page 28, lines 18-21, on page 32, lines 1-5, and on page 47, lines 25-28, of the specification.

Support for claims 622, and 667 can be found at least on page 30, lines 15-28, of the specification.

Support for claims 709-714 can be found at least on page 28, lines 18-21, and on page 32, lines 1-5, of the specification.

Support for claims 865-868 can be found at least on page 35, lines 9-11; on page 36, lines 10-15; and on page 37, lines 5-13, of the specification.

In regard to claim 666, the Applicant hereby reserves the right to submit claims in this or any related application to buffering agents in an amount equal to or less than 40 times the amount of the proton pump inhibitor on a weight to weight basis in the compositions. By amending this claim and the dependent claims, Applicant is in no way dedicating an amount of buffering agent equal to or less than 40 times the amount of the proton pump inhibitor to the public domain.

With entry of the above Supplemental Amendment and in view of the foregoing remarks, it is respectfully requested that pending claims 23, 27-35, 38-40, 42, 43, 52, 53, 65, 69, 73, 81, 84, 95, 96, 104-110, 112-123, 127-135, 622, 624-650, 652-654, 656, 661, 666, 667, 679-685,

687-704, 709-714, 716-719, 724, 725, 729-746, 757-759, 765, and 862-868 are in condition for allowance. Applicant respectfully requests early and favorable notification to that effect. The Examiner is encouraged to contact the undersigned with any questions or to otherwise expedite prosecution.

Respectfully requested,

THE CURATORS OF THE
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By: _____
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Version with Markings to Show Changes Made to the Claims

23. (Amended) A solid pharmaceutical composition in a dosage form that is not enteric-coated, comprising: active ingredients consisting essentially of:

(a) a non-enteric coated proton pump inhibitor [(PPI)] selected from the group consisting of omeprazole, lansoprazole, rabeprazole, esomeprazole, pantoprazole, pariprazole, and leminoprazole, or an enantiomer, isomer, derivative, free base, or salt thereof, in an amount of approximately 5 mg to approximately 300 mg; and

(b) at least one buffering agent in an amount [sufficient to prevent or inhibit acid degradation of the proton pump inhibitor (PPI) by gastric acid in a subject so as to achieve bioavailability of the proton pump inhibitor (PPI) in the subject after enteral administration of the dosage form;

wherein the dosage form is selected from the group consisting of a suspension tablet, a chewable tablet, an effervescent powder, and an effervescent tablet.] of approximately 0.1 mEq to approximately 2.5 mEq per mg of proton pump inhibitor; wherein the dosage form is selected from the group consisting of suspension tablet, chewable tablet, effervescent powder, and effervescent tablet.

95. (Amended) A method of treating an acid-related gastrointestinal disorder in a subject in need thereof, comprising: [enterally] administering to the subject the subject the dosage form of claim 23 via a route selected from the group consisting of oral, nasogastric, and gastric tube [a solid pharmaceutical composition in a dosage form that is not enteric-coated ,wherein the composition consists essentially of:

(a) a proton pump inhibitor (PPI) selected from the group consisting of omeprazole, lansoprazole, rabeprazole, esomeprazole, pantoprazole, pariprazole, and leminoprazole; and

(b) at least one buffering agent in an amount sufficient to prevent or inhibit acid degradation of the proton pump inhibitor (PPI) by gastric acid in the subject so as to achieve bioavailability of the proton pump inhibitor (PPI) in the subject after enteral administration of the dosage form].

96. (Amended) The method as recited in Claim 95, wherein the disorder is selected from the group consisting of duodenal ulcer disease, gastric ulcer disease, gastroesophageal reflux disease, erosive esophagitis, poorly responsive symptomatic gastroesophageal reflux

disease, pathological gastrointestinal hypersecretory disease, Zollinger Ellison Syndrome, and acid dyspepsia.

104. (Amended) The method as recited in Claim 95, wherein the [PPI] proton pump inhibitor is omeprazole.

105. (Amended) The method as recited in Claim 95, wherein the [PPI] proton pump inhibitor is lansoprazole.

106. (Amended) The method as recited in Claim 95, wherein the [PPI] proton pump inhibitor is rabeprazole.

107. (Amended) The method as recited in Claim 95, wherein the [PPI] proton pump inhibitor is esomeprazole.

108. (Amended) The method as recited in Claim 95, wherein the [PPI] proton pump inhibitor is pantoprazole.

109. (Amended) The method as recited in Claim 95, wherein the [PPI] proton pump inhibitor is pariprazole.

110. (Amended) The method as recited in Claim 95, wherein the [PPI] proton pump inhibitor is leminoprazole.

129. (Amended) The method as recited in Claim 95, wherein the buffering agent comprises at least one of calcium acetate, calcium glycerophosphate, calcium chloride, calcium hydroxide, calcium lactate, [calcium carbonate,] calcium bicarbonate, [calcium gluconate, calcium glycinate, calcium maleate, and] or other calcium salts.

132. (Amended) The method as recited in Claim 95, wherein the buffering agent is [comprises] about 250 mg to about 1000 mg calcium carbonate.

133. (Amended) The method as recited in Claim 95, wherein the buffering agent is [comprises] about 500 mg to about 1000 mg calcium carbonate.

622. (Amended) A method for treating an acid-related gastrointestinal disorder in a subject in need thereof, comprising: administering to the subject a solid pharmaceutical composition in a dosage form that is not enteric-coated[, consisting essentially of:]; wherein the composition comprises active ingredients consisting essentially of:

(a) a therapeutically effective amount of a non-enteric coated proton pump inhibitor selected from the group consisting of omeprazole, lansoprazole, rabeprazole, esomeprazole, pantoprazole, pariprazole, and leminoprazole, or an enantiomer, isomer, derivative, free base, or salt thereof; and

(b) a buffering agent selected from the group consisting of a bicarbonate salt of a group IA metal, a calcium salt, and a magnesium salt, wherein the buffering agent is in an amount sufficient to elevate gastric acid pH of the subject's stomach to prevent or inhibit gastric acid degradation of the non-enteric coated proton pump inhibitor and achieve sufficient [a mixture of sodium bicarbonate and a calcium salt, wherein the mixture is in an amount sufficient to prevent or inhibit acid degradation of the proton pump inhibitor by gastric acid in a subject so as to achieve] bioavailability of the proton pump inhibitor in the subject to elicit a therapeutic effect [after enteral administration of the dosage form].

624. (Amended) The [composition as recited in] method of Claim 622, wherein the calcium salt is selected from the group consisting of calcium acetate, calcium glycerophosphate, calcium chloride, calcium hydroxide, calcium lactate, calcium bicarbonate, [calcium gluconate, calcium glycinate, calcium maleate,] and other calcium salts.

625. (Amended) The [composition as recited in] method of Claim 622, wherein the sodium bicarbonate is in an amount from about 1000 mg to about 1680 mg.

626. (Amended) The [composition as recited in] method of Claim 622, wherein the sodium bicarbonate is in an amount of at least about 1680 mg.

627. (Amended) The [composition as recited in] method of Claim 622, wherein the calcium salt is calcium carbonate present in an amount from about 250 mg to about 1000 mg.

628. (Amended) The [composition as recited in] method of Claim 622, wherein the calcium salt is calcium carbonate present in an amount from about 500 mg to about 1000 mg.

629. (Amended) The [composition as recited in] method of Claim 622, wherein the calcium salt is calcium carbonate present in an amount of at least about 1000 mg.

630. (Amended) The [composition as recited in] method of Claim 622, wherein the [mixture] buffering agent is in an amount of at least 10 mEq.

631. (Amended) The [composition as recited in] method of Claim 622, wherein the [mixture] buffering agent is in an amount from about 10 mEq to about 70 mEq.

632. (Amended) The [composition as recited in] method of Claim 622, wherein the [mixture] buffering agent is in an amount from about 20 mEq to about 40 mEq.

633. (Amended) The [composition as recited in] method of Claim 622, wherein the proton pump inhibitor is in an amount from about 10 mg to about 100 mg.

634. (Amended) The [composition as recited in] method of Claim 622, wherein the proton pump inhibitor is omeprazole.

635. (Amended) The [composition as recited in] method of Claim 634, wherein the omeprazole is present in an amount of about 10 mg.

636. (Amended) The [composition as recited in] method of Claim 634, wherein the omeprazole is present in an amount of about 20 mg.

637. (Amended) The [composition as recited in] method of Claim 634, wherein the omeprazole is present in an amount of about 40 mg.

638. (Amended) The [composition as recited in] method of Claim 634, wherein the omeprazole is present in an amount of about 60 mg.

639. (Amended) The [composition as recited in] method of Claim 634, wherein the omeprazole is present in an amount of about 80 mg.

640. (Amended) The [composition as recited] method of in Claim 634, wherein the omeprazole is present in an amount of about 100 mg.

641. (Amended) The [composition as recited in] method of Claim 622, wherein the proton pump inhibitor is lansoprazole.

642. (Amended) The [composition as recited in] method of Claim 641, wherein the lansoprazole is present in an amount of about 15 mg.

643. (Amended) The [composition as recited in] method of Claim 641, wherein the lansoprazole is present in an amount of about 30 mg.

644. (Amended) The [composition as recited in] method of Claim 641, wherein the lansoprazole is present in an amount of about 45 mg.

645. (Amended) The [composition as recited in] method of Claim 641, wherein the lansoprazole is present in an amount of about 60 mg.

646. (Amended) The [composition as recited in] method of Claim 641, wherein the lansoprazole is present in an amount of about 90 mg.

647. (Amended) The [composition as recited in] method of Claim 641, wherein the lansoprazole is present in an amount of about 100 mg.

648. (Amended) The [composition as recited in] method of Claim 622, wherein the proton pump inhibitor is micronized.

649. (Amended) The [composition as recited in] method of Claim 622, wherein the composition is in a dosage form selected from the group consisting of a tablet, powder, suspension tablet, chewable tablet, capsule, effervescent powder, effervescent tablet, pellets, and granules.

650. (Amended) The [composition as recited in] method of Claim 622, wherein the subject is a human.

652. (Amended) The [composition as recited in] method of Claim 622, wherein the dosage form further comprises [comprising] a flavoring agent.

653. (Amended) The [composition as recited in] method of Claim 652, wherein the flavoring agent comprises aspartame, chocolate, root beer, peppermint, spearmint, [berry, peach,] or watermelon and combinations of any of the foregoing.

654. (Amended) The [composition as recited in] method of Claim 622, wherein the composition is provided as a separate component of a kit.

656. (Amended) The method [as recited in] of Claim [655] 622, wherein the disorder is selected from the group consisting of duodenal ulcer disease, gastric ulcer disease, gastroesophageal reflux disease [(GERD)], erosive esophagitis, poorly responsive symptomatic gastroesophageal reflux disease, pathological gastrointestinal hypersecretory disease, Zollinger Ellison Syndrome, and acid dyspepsia.

661. (Amended) The method [as recited in] of Claim [655] 622, wherein the dosage form [composition] is administered once or twice a day.

666. (Amended) A solid pharmaceutical composition in a dosage form that is not enteric-coated, comprising: active ingredients consisting essentially of:

(a) a therapeutically effective amount of a non-enteric coated proton pump inhibitor [(PPI)] selected from the group consisting of omeprazole, lansoprazole, rabeprazole, esomeprazole, pantoprazole, pariprazole, and leminoprazole, or an enantiomer, isomer, derivative, free base, or salt thereof; and

(b) a buffering agent selected from the group consisting of sodium bicarbonate and calcium carbonate, in an amount more than about [20] 40 times the amount of the proton pump inhibitor on a weight to weight basis in the composition.

667. (Amended) The composition as recited in Claim 666, wherein the amount of the buffering agent is sufficient for the agent to prevent or inhibit *in vivo* gastric acid degradation of the proton pump inhibitor upon the [enteral] administration of the dosage form to a subject so as to achieve bioavailability of the proton pump inhibitor in the subject.

680. (Amended) The composition as recited in Claim [679] 666, wherein the sodium bicarbonate is in an amount from about [1000] 400 mg to about [1680] 4000 mg.

681. (Amended) The composition as recited in Claim [679] 666, wherein the sodium bicarbonate is in an amount of at least about [1680] 800 mg.

682. (Amended) The composition as recited in Claim 666, wherein the buffering agent comprises calcium carbonate.

683. (Amended) The composition as recited in Claim [682] 666, wherein the calcium carbonate is in an amount from about [250] 400 mg to about [1000] 4000 mg.

685. (Amended) The composition as recited in Claim 682, wherein the calcium carbonate is in an amount of at least about 800 mg.

704. (Amended) The composition as recited in Claim 666, further comprising a flavoring agent[.] comprising aspartame, chocolate, root beer, peppermint, spearmint, [berry, peach,] or watermelon and combinations of any of the foregoing.

717. (Amended) A method of producing a liquid pharmaceutical composition comprising: combining [one or more of] the dosage form of Claim 666 [702] with an aqueous medium.

718. (Amended) A method for treating an acid-related gastrointestinal disorder in a subject in need thereof, comprising: [enterally] administering to the subject the dosage form [solid pharmaceutical composition] as recited in Claim 666 via a route selected from the group consisting of oral, nasogastric, and gastric tube.

719. (Amended) The method as recited in Claim 718, wherein the disorder is selected from the group consisting of duodenal ulcer disease, gastric ulcer disease, gastroesophageal reflux disease [(GERD)], erosive esophagitis, poorly responsive symptomatic gastroesophageal reflux disease, pathological gastrointestinal hypersecretory disease, Zollinger Ellison Syndrome, and acid dyspepsia.

745. (Amended) The composition as recited in Claim 34, wherein the flavoring agent comprises aspartame, chocolate, root beer, peppermint, spearmint, [berry, peach,] or watermelon and combinations of any of the foregoing.